MATERNAL NUTRITION AND ITS EFFECT ON THE OFFSPRING

Dietary, anthropometric, biochemical and haematological studies in urban Ethiopia

by

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Uppsala 1977

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This review is based on the following papers which will be referred to in the text by their Roman numbers.

I. Gebre-Medhin, M. and Gobezie, A.: Dieatary intake in the third trimester of pregnancy and birth weight of offspring among non-privileged and privileged women. Am. J. Clin. Nutr. 28:1322, 1975.

II. Gebre-Medhin, M.: Body weight changes during pregnancy in Ethiopian women.

III. Gebre-Medhin, M., Sterky, G. and Taube, A.: Observations on intrauterine growth in urban Ethiopia. Acta Paediatr. Scand. (Accepted for publication).

IV. Gebre-Medhin, M., Larsson, U., Lindblad, B.S. and Zetterström, R.: Subclinical evidence of protein-energy malnutrition in non-privileged Ethiopian mothers and their newborn infants. Acta Paediatr. Scand. (Accepted for publication).

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VI. Gebre-Medhin, M. and Vahlquist, A.: Vitamin A nutrition in the foetus.

VII. Gebre-Medhin, M., Vahlquist, A., Hofvander, Y., Uppsäll, L. and Vahlquist, B.: Breast milk composition in Ethiopian and Swedish mothers. I. Vitamin A and β-carotene. Am. J. Clin. Nutr. 29:441, 1976.

Introduction

For a number of reasons the role of nutrition in the health of the expectant mother and her newborn infant is a matter of particular interest to Third World countries. In these areas malnutrition is endemic (10, 23, 36, 55), fertility rates are high, young women enter the reproductive age early and subsequently attain high parities (22, 85). Health services are far from adequate and careful consideration has to be taken in the use of the meagre resources for action programmes (13). Gestation means a period of great strain for the mother as well as for the foetus. Maternal mortality rates are high and the incidences of foetal wastage, low birth weight (LBW $\leqslant$ 2500 g) and perinatal mortality are several times those reported for industrialized countries (11, 75, 86, 88).

The possibility that malnutrition during pregnancy might have a detrimental effect on the state of health of the foetus has generated extensive investigations in recent years (20, 45). In animals, to mention only a few examples from the vast amount of work carried out in this field, dietary restriction during gestation will limit litter size and retard subsequent growth (15), alter the morphology and histochemistry of foetal organs (93), and reduce the rate of cell multiplication in whole brain (92) and to a varying degree in specific brain regions (91).

In humans the evidence has been much less clear and the findings at times contradictory (3, 7, 16, 24, 85). This has been partly due to wide differences in the severity and the character of maternal malnutrition between the groups investigated. The discrepancies are particularly large when comparison is made between industrialized and less developed countries (78).

The often quoted data from the siege of Leningrad (1) and the famine in Holland during World War II (66) suggest that if birth weight alone is considered, severe food restric-

tion will result in a low birth weight. Similarly, evidence is accumulating that the high prevalence of LBW babies in developing countries is at least partly related to the nutritional status of the mothers (86). LBW babies born of low-income, presumably malnourished mothers show a marked reduction in the weight of all organs and histological examinations have revealed a general reduction in cell population (52). Chemical alterations have been observed in placentas of "small-for-dates" babies as well as in placentas from mothers considered to be malnourished (90), suggesting the possibility of impaired transfer of nutrients from mother to foetus.

Dietary evidence

With the exception of extreme situations such as outright famine, the question whether the diet taken by the mother during pregnancy itself affects the health, growth and development of the foetus is a debated subject (7). Many investigations have shown dietary inadequacies in relation to recommended levels in various population groups (16, 33). However, the interpretation of these findings is wrought with many problems. Dietary intakes show wide individual variations (33). Surveys have been carried out at different times during pregnancy and the methods used have not had the same level of precision (7, 33). The standards of evaluation of adequacy are not meant to provide a "yardstick against which to assess the diet of the individual woman" (33), but as a general guideline. The standards used have had varying "safety margins" (17, 56). The study population involved has often been small and has often consisted of hospital cases (80). In most of the dietary surveys reported, complete account has not been taken of these important intervening variables.

A few dietary intake studies have been carried out with care (47, 76), but the range of difference observed has often not been sufficiently large or has occurred above a level of dietary adequacy which would, in all probability, have little significance for foetal growth (26).

Clinical evidence

It would seem that the absence of convincing evidence of dietary inadequacies during pregnancy in various investigations is supported by the rarity of overt signs of *deficiency diseases* in the mother during this period. Although many studies, both in industrialized and Third World countries, show that the mortality and morbidity rates are higher among the socially disadvantaged, it has not been possible to establish a direct link between maternal diet and reproductive efficiency (33, 80, 87). A notable exception is iron deficiency (68), in some regions also folate deficiency (58), often giving anaemia of severe degree.

Anthropometric evidence

Regular observation of *weight changes during pregnancy* has long been a useful tool in the early diagnosis of perinatal problems (33, 75). A total weight gain of about 12 kg is associated with the lowest overall incidence of pre-eclampsia, low birth weight and perinatal mortality (75). Eastman and Jackson (18) and Simpson *et al.* (65) have clearly shown a rise in birth weight with increasing pregnancy weigh gain. However, weight changes during pregnancy show wide individual variations and, in addition to energy intake, are in-

fluenced by a number of other factors such as maternal age (14, 75), parity (31), pre-pregnancy weight (18), work out-put (84) and season (77). Available reports on this topic are difficult to compare and there are very few data from developing countries. Venkatachalam, Shankar and Gopalan (84) reported an average weight gain in non-privileged Indian women of 5.4 kg for primigravidae and 6.2 kg for multigravidae. These values are far below the level of 12 kg regarded as optimal in industrialized countries (75).

There is a wealth of literature comparing *birth weights* (and sometimes other anthropometric variables) in different population groups and regions of the world (33, 48). These studies have often shown a close relationship between socio-economic conditions, maternal diet and infant birth weight. Here again, however, there are many potential causes of variation in birth weight, that have not been explicitly investigated (7, 80). In some recent studies it has been found that the weight-specific perinatal mortality rates do not differ greatly between privileged and non-privileged groups but that the contribution of the non-privileged group to the higher total mortality arises from a greater proportion of LBW babies (87, 88). However, this does not resolve the question of why there is an increased proportion of LBW babies among the non-privileged.

By analysis of *intrauterine growth* patterns it is possible to study underlying factors in variations in birth weight and LBW rates in different population groups. Since Lubchenco and associates published their first paper (44), a number of investigations of intrauterine growth have been performed (73). Nearly all of these emanate from affluent societies and only a few have been undertaken in developing countries. Reports from India (8), Hong Kong (33), and Nigeria (79) show that newborns in these countries are lighter at all gestational ages in late pregnancy. However, since data on foetal growth in early gestation are difficult to interpret (73), it has not been possible to determine whether hitherto observed low values have been due to growth retardation as a result of malnutrition and other environmental factors, or to a uniform growth along a lower centile, in that case possibly reflecting genetic influence.

Some populations exhibit considerable differences in birth weight between first and subsequent parities (79). The effect of maternal age has been examined in some studies, which have shown an increase in birth weight with rising age (12, 21). In Aberdeen (78) the influence of socio-economic class on foetal growth was almost completely eliminated when the stature of the mother was taken into account. There are indications, at least in affluent countries (73), that the size of the mother, reflecting the effect of long term prematernal nutrition as opposed to gestational nutrition, may account for a major part of the differences in patterns of fetal growth observed between various population groups.

Biochemical evidence

In attempts at systematic investigations of gestational nutrition, apparently healthy women without clinically manifest signs of malnutrition have usually been examined. One method of selecting women for such studies has been routine biochemical tests on the blood and urine, which would exclude subjects with abnormal values. Kellner (39), Edozien (19), Stanier and Thompson (70), from

investigations among various population groups, have provided conflicting results about the levels of nutrients in the maternal blood and about foeto/maternal relationships. Furthermore, relatively low levels of several blood constituents such as haemoglobin, folate and serum proteins are regarded as normal for pregnancy (33). Hence, no reliable evidence of significant differences in levels of blood constituents between well and poorly nourished women is available.

Recently, Lindblad et al. (42, 43) investigated plasma concentrations of free amino acids in a "lower socio-economic group" consisting of 10 women from a refugee area in Karachi, and a "middle class group" consisting of 10 women delivered in a private hospital in the same town. Statistically significant changes were found in maternal and foetal plasma in the group mentioned first in the form of elevated non-essential amino acid levels and an increased glycine/valine ratio. These changes are identical to the changes found in moderate PEM* (30). It has been proposed that the increased glycine/valine ratio, which is characteristic of PEM in infants (67) and children (59), may be a valid indicator of malnutrition in pregnant women as well. Since the maternal glycine/valine ratio does not change during gestation or during hypertensive disorders, it may serve to distinguish between small-for-dates (SFD) babies whose small size is a result of maternal malnutrition, and truly premature infants and SFD infants whose smallness results from other causes. These observations are of considerable interest but should preferably be extended to other population groups, where more precise information about factors inherent in "low socio-economic life" is available.

Many surveys from subtropical and tropical countries have shown that *anaemia during pregnancy* is especially prevalent in non-privileged population groups (68). The common causes of the anaemia are dietary deficiencies, malabsorption, multiple pregnancies, blood losses, infections and parasitoses, and in certain areas haemoglobinopathies. However, the incidence of impaired reproductive efficiency in these areas is also high compared with the situation in industrialized countries. A WHO Expert Committee (87) reviewed reports linking maternal diet during pregnancy, among other entities, with gestational anaemia and the outcome of pregnancy, and found the evidence inconclusive.

The role of infection during pregnancy

The synergistic effects of *infection* and *malnutrition* in producing growth retardation and various other clinical syndromes affecting children have received increased recognition in recent years (60). It is also known that both clinically manifest and subclinical intrauterine infections may cause foetal growth retardation (62).

Many reports have focused attention on the effect of viral infections in relation to foetal growth (64). Antenatal bacterial infections have also been studied extensively (6). The presence of T-strains of mycoplasma (9) in the cervix or in the urine of the pregnant women, congenital syphilis (51) and positive seroconversion for toxoplasma during pregnancy has also been documented (63). However, reports on the relation of all these infections to gestational malnutrition are sparse.

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* protein-energy malnutrition

In Ethiopia, Larsson and Larsson (40) carried out serological screening for syphilis on a large number of pregnant women and their newborn infants attending a mother and child health (MCH) centre for the indigent in Addis Abeba. The test was positive in 15.3 % of the mothers. Half of the newborns of these seropositive mothers were also positive. Clinical signs including muco-cutaneous lesions, developed in 21.3 % of the infants of the 141 seropositive mothers who returned for follow-up. The incidence of stillbirths and abortions was stated to be significantly higher among these women than among the general population attending the same MCH centre. Until this report was issued, it had been stated that the clinical manifestations of congenital syphilis were extremely rare in Ethiopia (13).

In a recent report from a collaborative perinatal research project in Addis Abeba, Tafari et al. (72) stated that the amniotic fluid infection syndrome was a leading cause of perinatal mortality, accounting for over 30 % of the deaths. Dystocia ranked second (12 %) and syphilis third (8 %). Tafari et al. (72) showed that the pattern of diseases in the Ethiopian population was similar to that seen in industrialized countries up to the 34th week of gestation, after which the incidence of these diseases increased or remained high, while there was a tendency towards a decrease in industrialized countries. The infection rate was highest among poor gravida, in those engaged in hard physical work during pregnancy, and in twins. Examinations of amniotic fluid at term among the Ethiopian gravidae showed that 90 % lacked antimicrobial activity. The lack of this activity was correlated with socio-economic status and low zinc concentrations in the amniotic fluid.

The situation with respect to infections and their effect on foetal growth, health and survival has been commented upon in some detail. The reason is that—particularly in Third World countries—the overall risk of exposure to various kinds of infections is considerable (60). In the individual case it may be difficult to decide to what extent a small infant size in relation to gestational age is due to malnutrition or to infection. Where groups are concerned, and especially if effects of supplementary feeding to mothers during pregnancy are known, a correct interpretation of the situation will be more likely.

Dietary supplementation during pregnancy

In principle, it should be possible to elucidate the influence of gestational malnutrition on the mother and the offspring in feeding trials by providing dietary supplements to well defined groups with carefully documented dietary deficiencies. In practice such studies are difficult to carry out. Firstly, definite conclusions require large sample sizes, especially in industrialized countries, where only minor effects can be expected. Thomson (76), in an analysis of wartime experiences of feeding programmes for pregnant and lactating women in Great Britain, estimated that a feeding experiment would require more than 5000 subjects and a similar number of controls in order to prove a reduction in the incidence of stillbirths by 10 %. Secondly, such experimental studies would require a design which would verge on the unacceptable from the ethical standpoint (26). Thirdly, it is difficult in practice to carry out such experiments without at the same time providing benefits in the form of improved sanitation, medical care and other services (26).

Some such attempts have been made,

however. Two studies, one in India and one in Guatemala, deserve special mention. In the Indian study, Iyengar (34) supplemented 20 women of low socio-economic class who were admitted to hospital at the 36th week, their total diet providing 2300 Kcal and 80 g protein daily. The mean birth weight in this group was 3042 g. The birth weight in another group of women who did manual work and got no dietary supplement was 2633 g. However, no information is given about the general population from which the samples were taken or about other maternal characteristics. The hospitalized women were reported to have enjoyed other services and "considerable periods of bed rest" (34).

Habicht et al. (26) in Guatemala provided a dietary supplement to four Guatemalan Ladino villages, where previous investigations had shown the existence of considerable nutritional deficiencies. In two of the villages a gruel which supplements protein and energy was served and in the other two a cool drink which only supplies energy was provided. At the end of the follow-up an upward shift in the birth weight distribution was noted. For every 10,000 calories of supplement ingested by the mother during pregnancy the average birth weight was reported to have increased by 50 g. The increase in birth weight for the same amount of energy was not significantly different in women supplied with energy supplement alone and those who were given both protein and energy. This positive association between maternal energy supplementation and birth weight was observed irrespective of whether the supplement was ingested early or late in pregnancy. The statistical relation between supplemented energy during pregnancy and birth weight remained basically unchanged after the influence of maternal variables such as height, age and parity had been taken into account.

These findings suggest that under conditions of marked gestational malnutrition, improvement of the diet may have a measurable influence on foetal weight, although the mechanism of this effect is not known. The results require confirmation under other ecological conditions.

Foetal chemical development

The gross *morphological anatomy and the histology* of the human foetus during development have been studied in great detail (27). Extensive investigations of *chemical development* in utero have been undertaken by Widdowson and Spray (89). However, these studies relate to industrialized areas and there are extremely few data from those parts of the world where malnutrition is prevalent and successive pregnancies throughout the childbearing period are common.

Apte and Iyengar (2) reported on a study of the biochemical composition of a series of foetuses from mothers of low socio-economic groups in Hyderabad. It was found that up until 26 to 28 weeks of gestation this composition was similar to that of foetuses investigated in the United Kingdom (89). After that time the protein and fat contents of the Indian foetuses were considerably lower.

In a separate study, Iyengar and Apte (35) analysed the livers of most of the foetuses from this series in respect of vitamin A, vitamin B_{12}, folate, iron and copper. All these nutrients, but in particular vitamin A, showed extreme variations and in several livers the concentration of this vitamin was below 10 μg/g, which is lower than values reported elsewhere (50).

Human milk production and composition

The changing economic and social patterns associated with industrial development and urbanization have resulted in early cessation of breast feeding in favour of the bottle both in industrialized and developing countries in recent years (83). However, there are indications that in many areas this process is now being reversed as the uniqueness of human milk is being substantiated by new observations related both to the nutritional and the immunological fields (38). This trend has again generated interest in the influence of maternal nutrition on the *production* and *composition* of human milk. Quite a few studies on these matters have been carried out over the years (38). On the whole they indicate that whereas the production (ml/24 hr) is negatively influenced by poor maternal nutrition and health (25), the composition is much less affected.

Aims of the present investigation

A number of community surveys carried out in Ethiopia over the past two decades have all shown the existence of widespread malnutrition, especially in infants and children (5). However, no studies have so far been focused on the nutritional situation of pregnant and lactating women and their offspring. For this reason, and against the general background described in the Introduction it was considered of value to initiate an investigation with the following aims:

1. To collect information on dietary intake from a group of primigravidae during the third trimester of pregnancy.
2. To study the pattern of pregnancy weight gain in women representing different socio-economic groups.
3. To study the pattern of intrauterine growth in newborns representative of a wide range of socio-economic conditions.
4. To identify possible biochemical characteristics of malnutrition in mothers and their newborn babies.
5. To examine the haematological situation in mothers during pregnancy.
6. To compare the vitamin A nutrition in Ethiopian and Swedish newborns.
7. To compare the contents of vitamin A and β-carotene in milk obtained from Ethiopian and Swedish mothers.

Subjects investigated

The Ethiopian part of the survey was carried out at different maternal and child health clinics in Addis Ababa. In some of the studies the subjects were slected on the basis of their socio-economic status. A few of the clinics which provided services free of charge mainly catered for women whose family income rarely exceeded Eth$ 100 (Eth$ 1 = US$ 0.49) per month. Women belonging to this income group are referred to as non-privileged throughout this investigation. Their husbands had at most a year or two of primary school education, and the majority of the women themselves had none. Other clinics charged relatively high fees and their clientele, referred to here as privileged, had a family income generally above Eth$ 600 per month. In this category both spouses had acquired secondary school education and many were college graduates.

For the purpose of comparison some complementary data were collected in Sweden.

From the socio-economic, educational and nutritional standpoints, all the Swedish mothers in the present survey should be regarded as "privileged" in relation to the Ethiopian subjects.

An overall presentation of the subjects involved in the present investigation is given in Table 1.

Methods

The *dietary intake* of the individual woman was studied by use of the record technique on two consecutive weekdays. Further details of the procedures are given in paper I.

Anthropometric measurements were recorded by standard procedures (37).

Plasma amino acid analyses were performed by means of ion-exchange chromatography on a Bio-cal 200 (München) automatic analyser (69).

Haemoglobin concentration in the blood and *packed cell colume* were measured by the cyanmethaemoglobin and the MSE microhematocrit method, respectively. *Serum iron* and *serum transferrin* (TIBC) concentrations were determined according to the method of Richterich (57). *Folate* was estimated by the method described by Baker et al. (4) and modified by Hansen (28), and B_{12} as described by Hunter et al. (32).

The *vitamin A concentration in liver* samples was measured according to a modification of the method described by Thompson et al. (81), which is presented in detail in paper VI.

Retinol-binding protein (RBP) and *prealbumin* determinations were performed by the radial-immunodiffusion technique of Mancini et al. (46) as described in detail in paper VII.

Unless otherwise indicated, standard

Table 1. Overall presentation of all subjects involved in the present investigation

Study	Ethiopian			Swedish	Total
	Non-privileged	Privileged	Mixed		
I	20	10	–	–	30
II	–	–	294	–	294
III	–	–	3144	–	3144
IV	20(7[1])	5	–	–	32
V	117	44(75[3])	–	–	236
VI	39(62[2])	8	–	23(40[4])	179
VII	88	25	–	66	179
Total	360	167	3438	129	4094

[1] Newborn infants
[2] Apparantly healthy, liveborn infants
[3] Apparently healthy, non-pregnant control women
[4] Sudden deaths and accidents

statistical methods for the calculation of mean (M), standard deviation (SD), standard error (S.E.) and coefficient of correlation (r) were used.

Results

Dietary intake during pregnancy (I)

In the 30 women (20 non-privileged and 10 privileged) investigated the basic main meals were similar and consisted of *injera* and *wot*—a baked bread and a spiced stew—which are typical for highland parts of the country. The differences between the two groups lies mainly in the quantity and quality of the ingredients added to the *wot*. The non-privileged group added almost no animal protein or fresh vegetable and over 80 % of all the energy was derived from carbohydrates. In contrast, the *wot* consumed by the privileged women abounded in animal protein, fat and vegetables.

The percentage distribution of energy and nutrients in the diet of the two study groups as compared with the FAO/WHO recommendations is shown in Fig. 1. With the exception of iron and thiamine the non-privileged group consumed a diet that was grossly deficient in all respects. The previleged group met the recommendations for all nutrients except calcium and riboflavin.

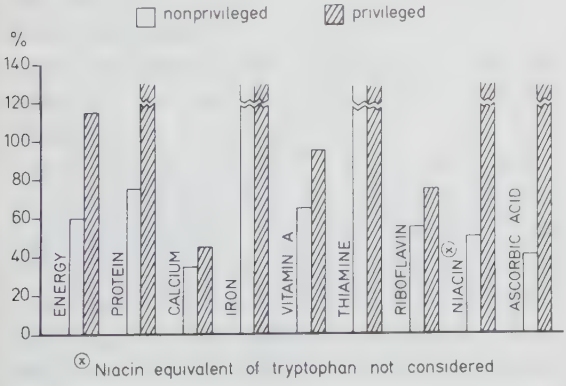

Fig. 1. Percentage adequacy of energy and nutrients compared with FAO/WHO recommendations.

The exceedingly high intake of dietary iron derives from the cereal *tef* (Eragrostis abbysinica Schrad), which is unique for the country and has a greater content of iron than other cereals (29), and in addition acquires a considerable amount of iron from the soil in the threshing process.

The mean daily intake of vitamin A by privileged women was 1124 μg and by non-privileged 808 μg. In the latter group, 30 % had an intake below 80 % of the FAO/WHO recommendations, and 35 % had an intake below 40 % of this recommended level.

Body weight changes during pregnancy (II)

Although the socio-economic situations of the non-privileged and privileged women differed greatly, no difference in antecendent weight, and only a slight one in height, was observed between these two groups. Primigravidae weighed significantly more than multigravidae ($p<0.05$) in early pregnancy.

A wide variation in weight gain was recorded in all the different income groups. Fig. 2 shows the distribution of mean weight gain for Ethiopian primigravidae compared with the pattern described by Thomson and Billewicz (75) for a large number of young primigravidae from Aberdeen.

The socio-economic status of the mother emerged as the most important determinant of pregnancy weight gain. Privileged women increased, on the average, 4.66 kg more than the non-privileged women ($p<0.001$). Fig. 3 presents the mean weight gain during

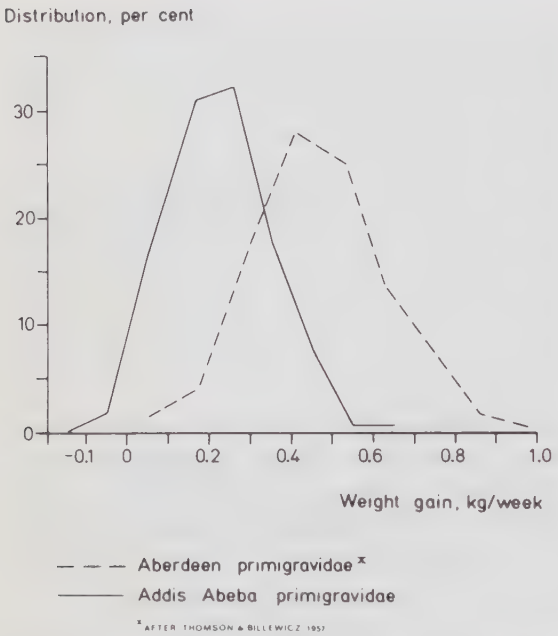

Fig. 2. Distribution of mean weight gain during pregnancy for Ethiopian primigravidae compared with Aberdeen primigravidae (75).

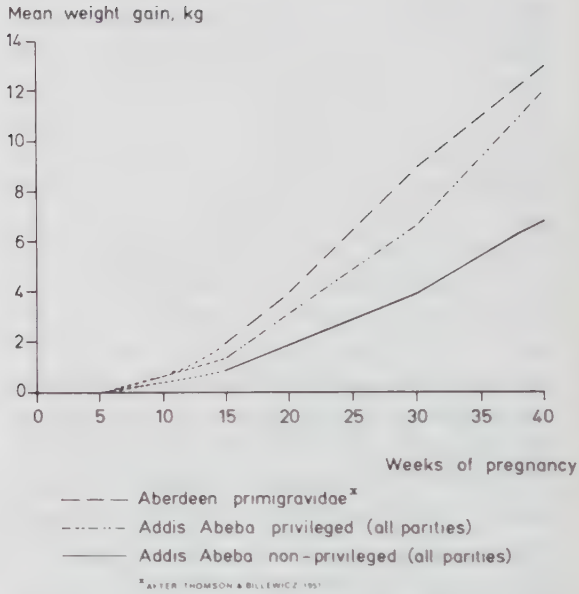

Fig. 3. Mean weight gain during pregnancy in privileged and non-privileged Ethiopian women compared with Aberdeen primigravidae (75).

pregnancy in some of the Ethiopian groups compared with the Aberdeen standard. Privileged Ethiopian women gained an amount close to this standard, while non-privileged women (all parities) and primigravidae (representing all income groups) increased 5.4 and 3 kg less, respec tively.

The differences in weight gain during pregnancy between the various Ethiopian groups showed no correlation to the antecedent weight or body height.

Pattern of intrauterine growth (III)

A comparison between Ethiopian and Swedish (71) newborns with respect to gestational age and anthropometric measurements is presented in Table 2. The mean length of gestation for Ethiopian newborns was 7.4 days shorter than the Swedish standard. On the average, Ethiopian boys weighed approximately 400 g less and girls 300 g less than Swedish newborns. The mean birth length of Ethiopian boys was 1.7 cm shorter and of girls 1.9 cm shorter. The mean head circumference at birth in Ethiopian boys was 1.5 cm smaller and in Ethiopian girls 1.0 cm smaller than a North American standard (54).

The pattern of anthropometric growth between the 34th and 43rd weeks of gestation is seen in Fig. 4. The median values for weight and length were close to the Swedish standard

Table 2. Birth weight, length and head circumference of Ethiopian infants compared with Swedish values (71). Mean ± SD are indicated

	Ethiopia		Sweden[1]	
	Boys n = 1682	Girls n = 1462	Boys	Girls
Length of gestation (days)	274.1 ± 13.6	273.3 ± 13.7	281.2 ± 13.5	281.2 ± 13.3
Birth weight (g)	3185 ± 465	3084 ± 411	3596 ± 542	3408 ± 503
Length (cm)	49.7 ± 2.0	49.4 ± 2.0	51.4 ± 2.4	50.3 ± 2.3
Head circumference (cm)	33.8 ± 1.8	33.7 ± 1.8	35.3[2]	34.7[2]

[1] (71)
[2] (54)

up to about 34–35 weeks. After that time very little further growth was recorded in Ethiopian infants.

Infants born to non-privileged mothers, women from the lowest income group, were on the average about 500 g lighter than those of the most privileged group ($p<0.05$).

The mean birth weight displayed a significant seasonal variation ($p<0.05$) between January and July. The lowest mean birth weights were noted for the months of January, February and March, i.e. from pregnancies commencing around April, May and June. For these pregnancies the third trimester coincided with the pre-harvest season, when staple foods are scarce and prices are customarily at a maximum.

Plasma levels of free amino acids in mother and newborn (IV)

The plasma aminogram of the non-privileged Ethiopian mothers during delivery and of their newborns displayed changes similar to those observed in the socio-economically similar, but ethnically different group of Pakistani

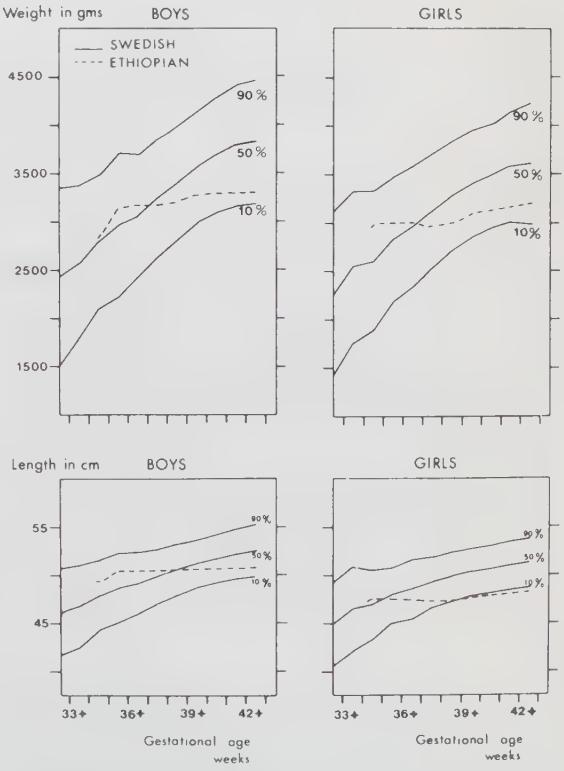

Fig. 4. Birth weight and birth length in relation to gestational age in Ethiopian infants compared with a Swedish standard (71).

women described by Lindblad et al. (42). The glycine levels and the glycine/valine ratio were significantly elevated in the maternal plasma during delivery and in the cord vein plasma in comparison with a normal Swedish material (41) (Fig. 5). In the newborn infant before initiation of feeding, there was a delay in the decrease of the branch-chained amino acids, particularly isoleucine. These findings suggest malnutrition *in utero*.

A reduced cord/maternal ratio of tyrosine and methionine was observed in the Ethiopian material, indicating placental dysfunction of unknown origin.

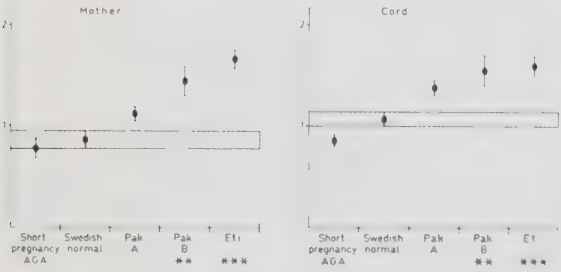

Fig. 5. The glycine/valine ratio during delivery. The maternal and cord plasma ratios of glycine/valine during delivery of the non-privileged Ethiopian group are compared with those of appropriate-for-gestational age (AGA) Swedish infants after a short pregnancy, those of normal Swedish deliveries (41), and those of two socio-economic groups (A = low socio-economic group and B = very low socio-economic group) in Pakistan (42). Mean ± SEM are indicated.
** = $0.001 < p \leqslant 0.01$, *** = $p \leqslant 0.001$.

Haematological values in pregnant women (V)

The haemoglobin concentration and packed cell volume (PCV) were investigated in three groups of Addis Ababa women towards the end of pregnancy. The values were compared with those in a control group of well-nourished nulliparous, regularly menstruating student nurses in Addis Ababa.

The mean Hb and PCV values were similar and within normal limits in all four groups regardless of their socio-economic status or parity. The results are presented in Table 3.

In one of the three study groups, non-privileged multiparae, the concentrations of iron, transferrin (TIBC), folate and vitamin B_{12} in the serum were also examined. All the individual folate and B_{12}-values and the means for S-iron and TIBC were within the normal range.

These findings indicate a rarity not only of true anaemia but also of 'physiological anaemia of pregnancy'.

Vitamin A nutrition in the foetus (VI)

Concentration of vitamin A in foetal livers. The mean, median and range of values for Ethiopian and Swedish foetuses are summarized in Table 4. The difference between the two groups is statistically highly significant ($p<0.001$).

Ethiopian foetal livers had lower concentrations of vitamin A than the Swedish ones at practically all gestational ages (Fig. 6). In both groups the vitamin A level seemingly increased with the duration of gestation.

Serum concentration of RBP. The mean serum concentration of RBP in liveborn, apparently healthy, Ethiopian infants was only slightly lower than the mean reported for Swedish infants. This finding suggests the existence of a mechanism for the protection of the foetus from vitamin A deficiency.

Vitamin A and β-carotene content of human milk (VII)

The concentration of vitamin A in the breast

Table 3. Hb, PCV and MCHC values in the last month of pregnancy in three groups of Ethiopian women as compared with a non-pregnant Ethiopian control group. Values within brackets indicate range

Category	n	Age (years)	Hb (g/dl)	PCV (%)	MCHC (%)
Primiparae privileged	44	23.4 (19–29)	13.4[1] (10.9–16.9)	41.7[5] (35–48)	32.5[5] (26.0–38.3)
Primiparae non-privileged	88	19.6 (15–28)	13.9[2] (8.7–19.4)	42.5 (26–50)	32.4 (27.1–42.4)[7]
Multiparae non-privileged	29	26.6 (19–40)	13.3[3] (11.7–14.6)	43.6[6] (38–51)	30.6[6] (25.6–35.5)
Controls	75	18.9 (17–23)	13.9[4] (11.1–19.4)	43.0 (38–48)	32.3[8] –

1 4 subjects with Hb below 11.8 g/dl
2 4 subjects with Hb below 11.8 g/dl
3 1 subject with Hb below 11.8 g/dl
4 2 subjects with Hb below 11.8 g/dl
5 n = 43
6 n = 25
7 The value 42.4 is probably due to a technical error. Only one more value is above 40.0
8 Calculated from mean values of Hb and PCV (individual values not accessible for this particular group when calculation of MCHC was performed)

Table 4. Concentrations of vitamin A in foetal liver

	Ethiopian	Swedish
	μg/g	
No.	49	23
Mean	33.3	64.6
Median	9.1	51.6
Range	0.2–168	7–237

milk and the content of vitamin A in a single milk feed were significantly higher ($p<0.05$) in the Swedish mothers than in the non-privileged Ethiopian mothers (Fig. 7).

The concentration of β-carotene in the milk and the content of β-carotene in single milk feed were significantly lower ($p<0.05$) in the Swedish mothers than in both the privileged and non-privileged Ethiopian mothers (Fig. 7).

The proportion of retinyl esters (percentage of total vitamin A content) in the milk was significantly higher in the Swedish mothers than in both privileged and, especially, non-privileged Ethiopian mothers.

The mean values for RBP in both groups of Ethiopian mothers were significantly lower ($p<0.001$) than in the Swedish mothers. In the non-privileged Ethiopian group 14/81 (17.2 %) manifested values below 20 μg/ml (i.e. 50 % of the normal), as opposed to 5 % in the privileged and none in the Swedish mothers.

Comments

The low energy and nutrient intake observed in the non-privileged gravidae conforms with the findings in dietary surveys carried out in several regions of Ethiopia over the past two

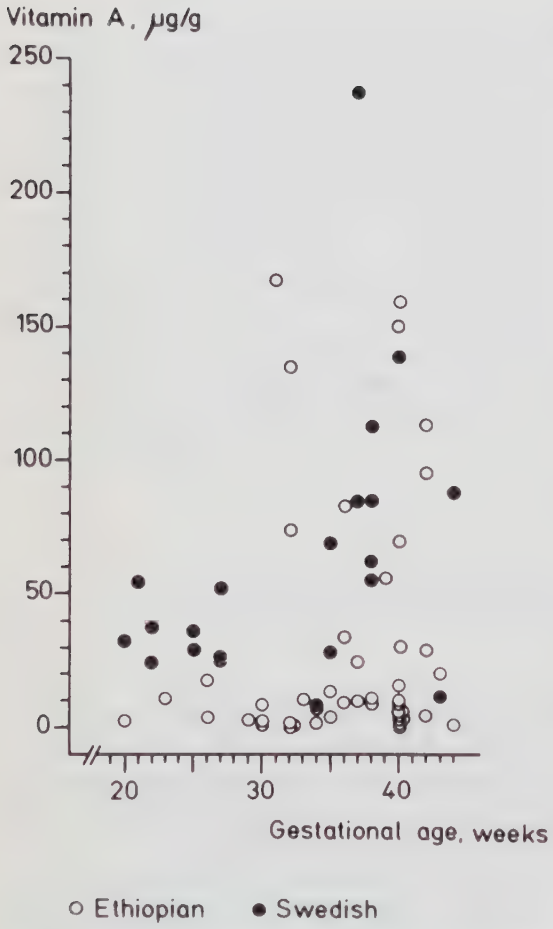

Fig. 6. Vitamin A concentration in foetal livers in relation to gestational age.

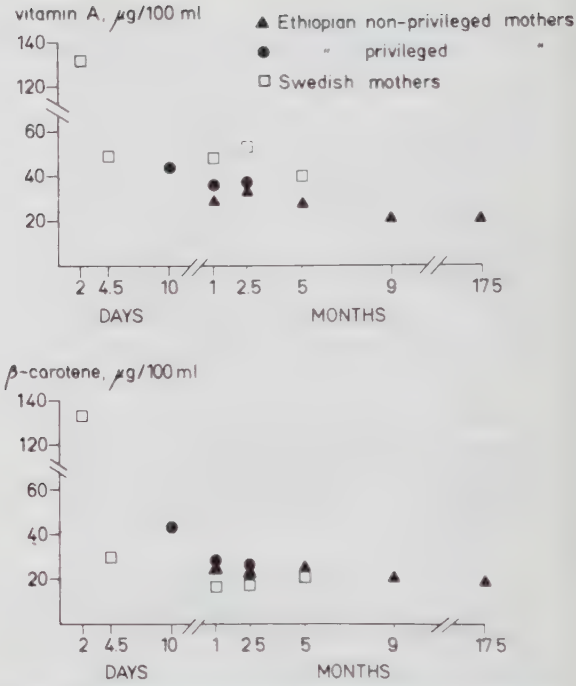

Fig. 7. Concentrations of vitamin A and β-carotene in breast milk at different times of lactation.

decades (49, 61). In this study the choice of well-defined socio-economic groups of apparently healthy, young primigravidae which were investigated simultaneously in the third trimester of pregnancy may be expected to enhance the validity of the differences observed between non-privileged and privileged groups. The considerable difference in dietary intake between the groups cannot be explained by variations in age, weight or stature as the women were essentially similar in these repsects.

The existence of this difference in dietary intake was reflected in the pattern of pregnancy weight gain. There is evidence that the difference in this pattern represents a discrepancy in the balance between energy intake and output (33). Thus, privileged women can afford to increase their energy intake or reduce their output in times of increased nutritional requirements.

The mean birth weight observed in this series is in agreement with results for much larger groups of Addis Ababa infants (22). In the present investigation birth weight displayed covariation with the socio-economic status of the mother, the lowest mean values being recorded for non-privileged groups.

Evidence was obtained in the present studies that the low mean birth weight for the total population investigated was a result of foetal growth retardation which was manifested at about 35 weeks of gestation. Since it is generally accepted that a close association exists between the dietary intake of the mother, on the one hand, and pregnancy weight gain and mean birth weight on the other, the observed growth retardation *in utero* strongly suggests the influence of gestational malnutrition. This is consistent with the plasma aminogram pattern, which showed signs indicating protein-energy malnutrition in the non-privileged group.

The low reserves of liver vitamin A early in gestation observed in Ethiopian foetuses suggest longstanding inadequacy of the nutrient supply. There was no difference in the liver vitamin A stores between foetuses who had died of infection and those who had succumbed from other conditions. This suggests a common etiological cause of the vitamin A deficiency, probably of a nutritional character. However, since signs of placental dysfunction (reduced cord/maternal ratio of some amino acids) were observed in non-privileged mothers, the possibility of this factor being of additional importance cannot be discounted.

The reduced levels of vitamin A in the milk and the lowered RBP concentrations in the serum observed in the non-privileged mothers demonstrate the continued detrimental effect of maternal malnutrition on the newborn infant.

This series of studies has shown that under the conditions ordinarily prevalent in a developing country, maternal nutrition during pregnancy is of critical importance for the growth and development of the offspring.

The results presented in this thesis pertain to urban dwellers with access to maternity and child health services. In Ethiopia the overwhelming majority of pregnant women do not get antenatal care, as the existing services are totally inadequate. This fact should be kept in mind in evaluating the results. It seems highly likely that the findings would be even more marked among the rural population.

Summary

1. A survey of the dietary intake of Ethiopian mothers in the third trimester of pregnancy showed that non-privileged women had an intake considerably lower than the recommended level, whereas the intake of the privileged women was in most instances equal to or in excess of this level.
2. The weight gain during pregnancy in non-privileged women was far below the amount regarded as optimal, whereas that in privileged women was close to this standard.
3. A slight curtailment of the gestational age was observed in Ethiopian infants as compared with the Swedish average. The intrauterine weight in Addis Ababa infants showed very little further increment after 34—35 weeks of gestation. Infants of non-privileged mothers had a significantly lower mean birth weight than those of privileged mothers. Birth weights showed variations in time during the course of the investigation, suggesting the effect of seasonal food shortage.
4. Non-privileged parturating mothers and their newborn infants displayed aberrations of the plasma free amino acids indicative of protein-energy malnutrition.

5. Anaemia of pregnancy which is widespread in many developing countries was found to be exceedingly rare in the population under study.
6. The liver concentrations and contents of vitamin A in Ethiopian foetuses were significantly lower than in Swedish foetuses.
7. Ethiopian mothers had a lower concentration and content of vitamin A but a higher content of β-carotene in their milk than Swedish mothers. In addition, non-privileged Ethiopian mothers had a lower concentration of retinol-binding protein in the serum than privileged Ethopian and Swedish mothers.

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